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NEW CHIRAL STATIONARY PHASES FOR OPTICAL RESOLUTION. OPTICALLY ACTIVE POLYAMIDES HAVING (-)-ANTI HEAD-TO-HEAD COUMARIN DIMER COMPONENT

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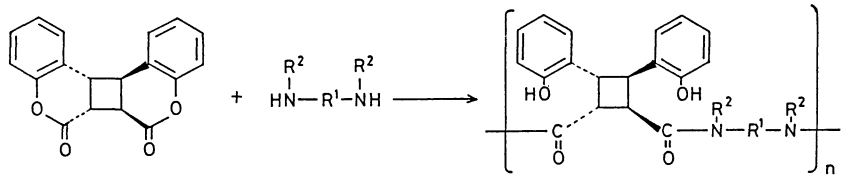
Optically active polyamides having (-)-anti head-to-head coumarin dimer component were found to be useful as chiral packing materials for direct HPLC resolution of enantiomers such as trans-stilbene oxide, mandelamide, benzyl mandelate, benzoin, trans-1,2-cyclobutanedicarboxanilide, and 2,2'-dihydroxy-1,1'-binaphthyl.

With the increasing demand for optically active compounds in many fields, the need for rapid resolution of enantiomers with high enantiomeric purity has prompted to develop new resolution methods. One solution to such a problem would be the direct HPLC separation of the enantiomers upon a column packed with a suitable chiral stationary phase.[1] For a low-molecular-weight chiral stationary phase, chiral recognition requires at least three simultaneous interactions between the chiral stationary phase and at least one of the solute enantiomers.[2] In most polymeric chiral stationary phases such as poly(triphenylmethyl methacrylate),[3] natural polypeptides,[4] and modified cellulose,[5] chiral recognition depends strongly on the secondary or higher-ordered structure of the polymer. The chiral recognition by cross-linked polyacrylamides with chiral pendant groups seems due to the contribution of hydrogen-bonding.[6] No report can be found of the application of synthetic polymers having asymmetric centers in the main chain as chiral stationary phases for HPLC. Below, we describe a successful application of optically active polyamides, which have an optically active component in the main chain, as new stationary phases for HPLC. These polymers act on solutes by several interactions or by conformational constraint.

We have synthesized optically active polyamides composed of (-)-anti head-to-head coumarin dimer subunit, which possess three possible interaction sites for chiral recognition, i.e., the phenolic hydroxyl group, the aromatic group, and the amide linkage. Moreover, by varying the rigidity of diamine component, the secondary structure of these polyamides can also be controlled to some extents.[7] As expected, these polyamides could resolve completely or partially enantiomers **5-10** having aromatic groups. Simultaneous three-point interactions and highly-ordered conformations of these polyamides seem to contribute to the

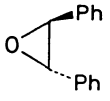


Polyamide	R^1	R^2
1	$-(CH_2)_6-$	H
2		H
3		
4	$-(CH_2)_6-$	CH_3

chiral recognition ability, depending on the structure of diamine components.

The polyamides **1-4** were prepared by a ring-opening polyaddition reaction in DMAc at 80 °C.[7] TG-DSC analyses indicated that these polyamides are almost amorphous polymers with softening points higher than 250 °C in a nitrogen stream. Macroporous silica gel,[8] pretreated with diphenylsilane coupler, was coated with about 25 wt% of the polyamide in DMAc. The modified silica gel was packed in a stainless steel column [250 mm x 4.6 (i.d.) mm] by the slurry method.[9]

Fig. 1 shows the chromatographic resolution of benzoin (**8**), trans-1,2-cyclobutanedicarboxanilide (**9**), and 2,2'-dihydroxy-1,1'-binaphthyl (**10**), on columns bearing polyamides **1**, **2**, and **3**, respectively. The chromatographic parameters for the resolution of these compounds and **5-7** using the polyamide columns are summarized in Table 1. The chiral discrimination by these chiral stationary phases was highly dependent on the diamine component of the main chain. A polyamide derived from a aliphatic diamine (**1**) resolved **5**, **6**, and **8** with high efficiency, while polyamide **2** resolved **9** and polyamide **3** resolved **10** with high capacity factor (α= 1.81 and 1.63, respectively). Enantiomers **5**, **6**, **7**, and **8**, which all contain a phenyl group and possess a site for hydrogen-bonding, were successfully resolved by **1**. However, **4** showed no resolving ability for these compounds, due to the lack of amide-hydrogen. These results indicate that the chiral discrimination of **1** should involve simultaneous interactions of aromatic stacking and hydrogen-bonding with the solutes. The unique resolving power of **2** for **9** can be due to the high-ordered conformation of **2**, that makes the hydrophobic interaction of aromatic groups of **2** with the propellar-like phenyl groups of **9** suitable for only one of the enantiomers. The high chiral discrimination of **3** for **10** may also be attributed to its highly-ordered conformation, which can in turn be attributed to its very tight and rigid polymer main chain.[7] These non-polar, highly-ordered conformation-dependent interactions can not found in **1** and **4** due to their highly flexible main chain.



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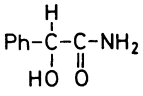

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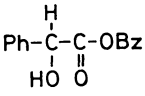

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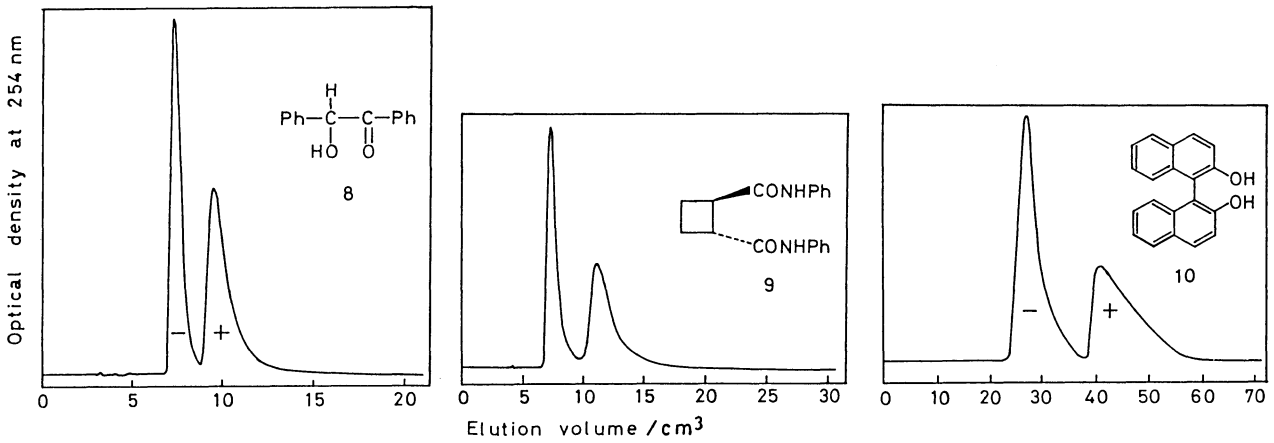

Fig. 1. Chromatographic resolution of **8**, **9**, and **10** on the columns of **1**, **2**, and **3**, respectively.

Table 1. Chromatographic Resolution of **5**-**10**[a)]

	Column bearing **1**			Column bearing **2**			Column bearing **3**		
Compd	k'_1	α	Rs	k'_1	α	Rs	k'_1	α	Rs
5	0.40	1.42	0.92	0.41	1	-	0.64(-)	1	-
6	5.59(-)	1.29	0.88	8.04(+)	1.03	0.50			
7	1.60	1.10	0.60	1.68(-)	1.05	0.50	3.12(-)	1.04	0.50
8	1.91	1.46	1.45	2.16	1	-	4.17(+)	1	-
9	1.40	1	-	2.00	1.81	1.73	3.30	1	-
10	4.36(-)	1.17	-	2.19	1	-	9.91(-)	1.63	1.19

a) Eluent, hexane/2-propanol (v/v = 9/1); flow rate, 0.50 cm^3/min. k'_1 (capacity factor for less retained enantiomer) = (retention volume - dead volume)/dead volume. α (separation factor) = (capacity factor for more retained enantiomer)/k'_1. Rs (resolution factor) = 2 x (distance of the two peak position)/(sum of band-widths of the two peaks). The sign in the parentheses is that of optical rotation at 365 nm.

The present results indicate that optically active polyamides derived from anti head-to-head coumarin dimer and various diamines will provide useful chiral packing materials. The relationships between their main chain structure and resolution power also provide insights into the elucidation of the chiral discrimination mechanism.

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8) Macroporous spherical silica gel has 10 μm of mean particle size with 100 nm of mean pore diameter and 20000 m^2/kg of specific surface area.

9) Theoretical plate numbers of the column **1**, **2**, **3**, and **4** for benzene were 2600, 2200, 2100, and 2800, respectively, at a flow rate of 0.50 cm^3/min.

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